

Innovation in Risk Assessment- Using Time-Dependent Models to Interpret Neurobehavioral Toxicity Studies

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2

Development of Time-Dependent Models for Application to Neurotoxicity Data

The dose-response modeling of neurobehavioral data poses challenges that include handling data with repeated measurements over time, multiple endpoints with both continuous and ordinal scales, and time dependence of risk characterization. To address these and other issues, the Agency has developed new statistical methods and models for the estimation of benchmark doses (BMDs) from such time-dependent studies. An external peer review of these methods and models was conducted in December of 2003. This poster illustrates the application of these models to one particular continuous endpoint, hindlimb grip strength.

3

Hindlimb Grip Strength Example

Figure 1

- Depicts the change in hindlimb grip strength in rats over time, after a single exposure to triethyl tin bromide (TET)

Figure 2

- 3D spline plot of the relationship between time, dose and grip strength
- Exposure to TET resulted in decreases in strength at 2H and 24H as compared to control
- At the end of one week average hindlimb grip strength recovered to baseline except in the highest dose group (~ 75% recovery)

Figure 1b. Change of Hindlimb Grip Strength in Rats after a Single Exposure to TET (Log-scale of time)

